

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) An isolated oligonucleotide that:

(a) ~~comprises~~ consists of a nucleotide sequence that is complementary to a strand of a genomic a-region consisting of:

(i) at least a portion of the central repeat unit of three repeat units composing a tandem repeat in the promoter region of ~~the a human~~ thymidylate synthase gene, and

(ii) at least a portion of the repeat unit located downstream of the central repeat unit[,,,]; and

~~and~~(b) hybridizes to the genomic region of (a) under highly stringent hybridization conditions.

2. (Currently amended) The ~~isolated polynucleotide~~ oligonucleotide of claim 1, wherein ~~the nucleotide hybridizes to the 3' end repeat unit of the two repeat units composing a tandem repeat in the promoter region of the thymidylate synthase gene,~~ under hybridization conditions that are less stringent than the highly stringent conditions of (b), the oligonucleotide can hybridize either to the genomic region of (a) or instead to a second region, the sequence of which consists of the sequence of at least a portion of the downstream repeat unit of (a)(ii).

3. (Currently amended) The ~~isolated~~ oligonucleotide of claim 2, wherein the ~~nucleotide sequence~~ oligonucleotide comprises the nucleotide sequence of ~~SEQ ID NO: 2~~SEQ ID NO:1.

4. (Currently amended) An isolated oligonucleotide consisting of a sequence that is complementary to and hybridizes under highly stringent hybridization conditions to either strand

of a first genomic region in the promoter region of a human thymidylate synthase gene, the first genomic region being upstream of a second genomic that hybridizes to the region adjacent to 5' side of the oligonucleotide that

(a) comprises a nucleotide sequence that is complementary to a region consisting of [[:]]

(i) at least a portion of the central repeat unit of three repeat units composing a tandem repeat in the promoter region of the thymidylate synthase gene, and

(ii) the repeat unit located downstream of the central repeat unit, and

(b) hybridizes to the region of (a).

5. (Currently amended) The isolated oligonucleotide of claim 4, wherein the nucleotide sequence of the oligonucleotide comprises the nucleotide sequence of SEQ ID NO:1 SEQ ID NO:2.

6. (Currently amended) A method for identifying the number of tandem repeats in the promoter region of ~~the a human~~ thymidylate synthase gene, the method comprising:

(a) amplifying a section of genomic DNA that comprises tandem repeats in at least the promoter region of the thymidylate synthase gene, to produce an amplified genomic DNA;

(b) ~~hybridizing~~ contacting the oligonucleotide of claim 1 [[to]] with the amplified genomic DNA ~~of step (a)~~ under the highly stringent hybridization conditions~~[[,]]~~;

(c) detecting [[a]] whether hybridization between the oligonucleotide and the amplified genomic DNA has occurred~~[[,]]~~ and

(d) identifying the number of tandem repeats as “two” when hybridization is not detected, and identifying the number of tandem repeats as “three” when hybridization is detected~~[[,]]~~.

7. (Currently amended) The method of claim 6, further comprising:

(e) ~~hybridization~~ contacting the oligonucleotide of claim 1 [[to]] with the amplified genomic DNA ~~of step (a)~~ under hybridization conditions that are less stringent than the highly stringent hybridization conditions~~;(b);~~

(f) detecting [[a]] whether hybridization between the oligonucleotide and the genomic DNA has occurred under the less stringent conditions;[[,]] and

(g) identifying the number of tandem repeats as "two" when hybridization is not detected under the highly stringent conditions in (e) but is detected under the less stringent conditions in (f);

8. (Currently amended) The method of claim 6, wherein the ~~hybridization is detected by~~ detection step comprises a melting curve analysis.

9. (Currently amended) The method of claim ~~[[8]]~~6, the method comprising the step of detecting fluorescence resonance energy transfer using (i) the oligonucleotide, labeled at its upstream end with a first fluorescent dye; and of claim 4, wherein the 3' end of the oligonucleotide is labeled with a fluorescent dye, and (ii) the oligonucleotide of claim 1 whose 5' end is labeled with a different fluorescent dye that transfers fluorescence resonance energy to the fluorescent dye at the 3' end of the oligonucleotide of (i) (ii) a second oligonucleotide that hybridizes to a second region within the tandem repeat region adjacent to and upstream of the genomic region, wherein the second oligonucleotide is labeled at its downstream end with a second fluorescent dye, and wherein when the two fluorescent dyes are proximal to each other, either the first fluorescent dye transfers fluorescence resonance energy to the second fluorescent dye or the second fluorescent dye transfers fluorescence resonance energy to the first fluorescent dye.

10. (Currently amended) The method of claim 9, wherein the second oligonucleotide of (ii) comprises the nucleotide sequence of SEQ ID NO: 2.

11. (Currently amended) The method of claim 10, wherein the first oligonucleotide of (i) comprises the nucleotide sequence of SEQ ID NO: 1.

12. (Currently amended) The method of claim 9, wherein the two fluorescent dyes are, respectively, that labels the oligonucleotide of (i) is FITC and either, and the fluorescent dye that labels the oligonucleotide of (ii) is RED640 or RED705.

13. (Original) A method for genotyping the thymidylate synthase genealleles of a subject, the method comprising:

(a) identifying the number of tandem repeats in the promoter region of the subject's thymidylate synthase genealleles by the method of claim 6, and

(b) determining that the thymidylate synthase genotype of the subject is "homozygous 2R/2R" when the number of tandem repeats is identified as only "two," "homozygous 3R/3R" when the number of tandem repeats is identified as only "three," or "heterozygous 2R/3R" when the number of tandem repeats is identified as both "two" and "three".

14. (Original) A method for predicting the responsiveness of a subject towards an antitumor agent targeting thymidylate synthase, the method comprising:

(a) determining the thymidylate synthase genotype of the subject by the method of claim 13, and

(b) associating the thymidylate synthase genotype with the responsiveness of the subject towards an antitumor agent targeting thymidylate synthase.

15. (Currently amended) A method for determining the dose and/or the type of an antitumor agent targeting thymidylate synthase for treating a cancer patient, the method comprising:

(a) determining the thymidylate synthase genotype of the patient by the method of claim 13, and

(b) for a "homozygous 2R/2R" patient, deciding either to: (i) administer a dose of an antitumor agent dose targeting thymidylate synthase that is lower than the normally used dose of that agent, or (ii) use an antitumor agent that has a different target.

16. (Currently amended) A kit for identifying the number of tandem repeats in the promoter region of ~~the a human~~ thymidylate synthase gene, the kit comprising:

~~(i) the oligonucleotide of claim 4, and~~

~~(ii) the oligonucleotide of claim 1~~

(A) a first oligonucleotide comprising a nucleotide sequence that is complementary to a strand of a genomic region consisting of:

(i) at least a portion of the central repeat unit of three repeat units composing a tandem repeat in the promoter region, and

(ii) at least a portion of the repeat unit located downstream of the central repeat unit,

wherein the first oligonucleotide hybridizes to the genomic region under highly stringent hybridization conditions; and

(B) a second oligonucleotide that hybridizes to a region adjacent to and upstream of the first oligonucleotide under the highly stringent hybridization conditions.

17. (Currently amended) The kit of claim 16, wherein the downstream[[3']] end of the second oligonucleotide ~~of (i)~~ is labeled with FITC, and the upstream[[5']] end of the first oligonucleotide ~~of (ii)~~ is labeled with the fluorescent dye RED640 or RED705.

18. (Currently amended) The kit of claim 16, wherein the first oligonucleotide comprises~~the kit comprising:~~

(a) an oligonucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or the complement thereof, and the second oligonucleotide comprises

(b) an oligonucleotide comprising the nucleotide sequence of SEQ ID NO: 2 or the complement thereof.

19. (New) A kit comprising

(a) a first oligonucleotide consisting of the nucleotide sequence of SEQ ID NO:1 or the complement thereof; and

(b) a second oligonucleotide consisting of the nucleotide sequence of SEQ ID NO:2 or the complement thereof,  
each of the oligonucleotides being optionally labeled with a fluorescent dye.

20. (New) An isolated oligonucleotide comprising a nucleotide sequence complementary to a genomic region consisting of:

(i) at least a portion of the central repeat unit of three repeat units composing a tandem repeat in the promoter region of a human thymidylate synthase gene, and

(ii) at least a portion of the repeat unit located downstream of the central repeat unit, wherein the oligonucleotide hybridizes to the genomic region under highly stringent hybridization conditions, and wherein the upstream end of the oligonucleotide is labeled with a fluorescent dye.

21. (New) The oligonucleotide of claim 20, wherein the nucleotide sequence of the oligonucleotide consists of the sequence complementary to the genomic region.

22. (New) An isolated oligonucleotide that is complementary to and hybridizes under highly stringent hybridization conditions to either strand of a first genomic region, the first genomic region being adjacent to and upstream of a second genomic region consisting of at least a portion of the central repeat unit of three repeat units composing a tandem repeat in the promoter region of a human thymidylate synthase gene, wherein the downstream end of the oligonucleotide is labeled with a fluorescent dye.

23. (New) An oligonucleotide consisting of the sequence of SEQ ID NO:1, the oligonucleotide being optionally labeled with a detectable label.

24. (New) An oligonucleotide consisting of the sequence of SEQ ID NO:2, the oligonucleotide being optionally labeled with a detectable label.